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## REMARKS

Reconsideration of this application is respectfully requested in view of the foregoing amendment and the following remarks.

Among the inventions disclosed in the instant specification, Applicants discovered that anthrax B moieties having a mutation that inhibits pore-formation are useful as an antidote to particular bacterial infections. Applicants' claims are directed to anthrax B moieties comprising a D425K mutation that the Examiner has indicated is free of prior art (claims 1, 52-55, and 56-60), and to immunogenic compositions comprising such anthrax B moieties (claims 6 and 61-64). Given their demonstrated ability to interfere with the pore-formation of naturally-occurring B moieties, such compositions are useful not only as prophylactics, but also as therapeutics.

Summary of Office Action

Examination of claims 1-4, 6-8, 12-20, 29-31, 33-35, and 40-51 is reported in the present Office Action. Claims 1, 6, 8, 12, 15, 20, and 33 are rejected under the judicially created doctrine of obviousness-type double patenting. Claims 1-4, 6-8, 12-20, 29-31, 33-35, 40-42, and 45-47 are rejected under 35 U.S.C. § 112, first paragraph. Claims 1-4, 6-8, 12-20, 29-31, 33-35, 42, 45, and 46 are rejected under 35 U.S.C. 102(a); claims 1-4, 6-8, 12, 13, 15, 18-20, 29-31, 33-35, 42, 45, and 46 are rejected under 35 U.S.C. 102(e); claims 1-4, 5-8, 12-20, 29-31, 33-35, 42, 43, 45, and 46 are rejected under 35 U.S.C. 102(b). Claims 1-4, 12-20, 40, 41, 50, and 51 were rejected under 35 U.S.C. § 101. Claims 1, 12, 30, 33, 40, 41, and 47 are rejected under 35 U.S.C. § 112, second paragraph. Claims 43-44, 49, 50a-g, i, m, n, p, q, 51 d, f, g, i, and j are withdrawn. Each of the rejections is addressed below.

Support for the Amendment

Support for the amendment of claims 1 and 6 and for new claims 52-64 is found throughout the specification and claims as originally filed. For example, support for the amendment of claims 1 and 6 and for new claims 52-64, which recite specific sequence identifiers, is found, for example, in the Sequence Listing and in Table 1; support for the amendment of claim 6 and new claims 61-64, which recite immunogenic compositions, is found, for example, in the instant specification at page 13, lines 15-19; page 17, lines 25 and 26; and at page 22, lines 19-26; and support for new claim 55, which recites a

quadruple mutation including ΔD2L2, where ΔD2L2 denotes deletion of amino acids 302-325, is found, for example, at page 23, line 20.

As an initial matter, Applicants respectfully disagree with the present rejections. However, in order to expedite issuance of certain claims covering subject inventions that Examiner has indicated to be allowable, applicants have amended the pending claims. This amendment should not be construed as acquiescence to the Examiner's position and applicants reserve the right to pursue all canceled subject matter in this, or future, related applications.

Claims Directed to Unexamined Subject Matter

The Examiner asserts that new claims 43-44, 48-49, 50 a-g, i, m, n, p, and q, and 51 d, f, g, i, and j are distinct from the originally examined invention. Applicants note that the present amendment cancels these claims.

Rejections under 35 U.S.C. § 102(a)

The Examiner indicated that the Declaration of Dr. R. John Collier was believed to be ineffective in overcoming the rejection under 35 U.S.C. 102(a) over WO 99/42473. Claims 1 and 6 and new claims 52-64 are directed to compositions featuring anthrax B moieties (SEQ ID NOs:8, 10, 11, 13, and 16) that contain a D425K mutation. As the Examiner has now indicated that the D425K mutation is free of prior art, the Declaration of Dr. R. John Collier is no longer relevant. Applicants respectfully request that the

rejection be withdrawn.

Obviousness-type Double Patenting

Claims 1, 6, 12, and 33 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1 and 4-7 of Collier et al. (U.S. Patent No. 6,455,673); and claims 1, 6, 8, 12, 15, and 33 are rejected over claims 1-13 and 23-27 of Collier et al. (U.S. Patent 5,917,017). Because the claims now recite the D425K mutation, these two rejections are no longer applicable and Applicants respectfully request that the obviousness-type double patenting rejections be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

*Written description*

Claims 1-4, 6-8, 12-20, 29-31, 33-35, 40, 41, 47, 50, and 51 are rejected for lack of an adequate written description.

Applicants note that claims 2-4, 6-8, 12-20, 29-31, 33-35, 40, 41, 47, 50, and 51 have been cancelled.

The claims now recite anthrax toxin B moieties containing the D425K mutation that the Examiner has indicated to be allowable. Specifically, claim 1 and new claims 52-55 are directed to anthrax toxin B moieties having at least 95% amino acid sequence identity to SEQ ID NOs:8, 10, 11, 13, and 16, which contain a D425K mutation; claims 52-55 are directed to polypeptides comprising SEQ ID NOs:8, 10, 11, 13, and 16; and

claims 6 and 61-64 are directed to immunogenic compositions containing anthrax toxin B moieties of the invention.

The specification at Table 1 explicitly describes exemplary anthrax toxin B moieties having: a D425 mutation (SEQ ID NO:8); a D425K mutation in combination with K397D (SEQ ID NO:10); a D425K mutation in combination with K397D and F427A (SEQ ID NO:13); a D425K mutation in combination with K395D, K397D and D426K (SEQ ID NO:11) ; and a D425K mutation in combination with K397D, F427A, and ΔD2L2 (SEQ ID NO:16).

With respect to new claims 61-64, which feature immunogenic compositions that recite SEQ ID NOs:8, 10, 11, 13, and 16, the instant specification explicitly describes exemplary anthrax toxin B moieties containing mutations that are useful for the induction of an immune response (page 19, line 8, to page 19, line 18). The instant specification also demonstrates that exemplary anthrax toxin B moieties containing a mutation (e.g., those identified in Table 1) can induce the production of protective antibodies and inhibit the activity of PA from the infecting bacteria (page 18, line 12, to page 19, line 18; page 22, line 19, to page 23, line 4). The instant specification provides exemplary anthrax toxin B moieties containing a mutation (e.g., the D2L2 deletion mutant, K397D + D425K, and F427A mutants) exhibit little or no diminution in immunogenicity relative to wild-type PA in rats and demonstrates that these exemplary mutants are not only capable of inducing an immune response but are also protective against wild-type toxin administration in a rat model of anthrax (page 22, lines 22-26, and pages 37-41).

In summary, the present specification explicitly describes immunogenic compositions featuring anthrax toxin B moieties that include a mutation at D425K. Accordingly, Applicants respectfully request that the § 112, first paragraph, rejection be withdrawn.

*Enablement*

Claims 6-8, 33-35, 42, and 45-57 are rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Specifically, the Examiner asserts that the use of a vaccine composition to protect against infection with a viable bacteria is unpredictable.

Applicants note that claims 7, 8, 33-35, 42, and 45-57 have been cancelled. Claims 6 and new claims 61-64 recite immunogenic compositions that feature purified anthrax toxin B moieties containing SEQ ID NOs:8, 10, 11, 13, or 16, each of which contains a D425K mutation.

The instant specification at pages 39 and 40 provides working examples showing that exemplary anthrax toxin B moieties containing a mutation (e.g., K397D + D425K, F427A, or D2L2) induce a protective immune response in a vaccinated rat. The administration of the mutant B moiety induces an immune response and allows the rat to survive injection with a lethal dose of anthrax toxin. See pages 39-40, and Table 5 of the specification.

The instant specification also points out that desirable mutants identified in this manner can be characterized in well-known animal models (page 46, lines 9-11, and page

48, lines 7-10), and provides methods for assaying for an immune response (pages 39-40). Thus, applicants have clearly enabled the full scope of the invention as presently claimed. Applicants respectfully request withdrawal of the enablement rejection.

Rejections under 35 U.S.C. § 102

Claims 1, 6, 8, 12, 15, and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Collier et al. (U.S. Patent No. 5,917,017); claims 1-4, 6-8, 12, 13, 15, 19, 20, 29-31, and 33-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Cirino et al. (U.S. Patent No. 6,329,156); claims 1, 3, 5, 6, 8, 12, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (U.S. Patent No. 5,792,458); claims 1-3, 5-8, 12-18, and 31 are rejected under 35 U.S.C. 102(b) as anticipated by Singh et al. (J. Biol. Chem. 269: 29039-29046, 1994); claims 1-3, 4, 6-8, 12-20, 29-31, and 33-35 are rejected under 35 U.S.C. 102(b) as anticipated by Miller et al. (Abstract 712-M); and finally, claims 1-3, 5-8, 12-18, 29, 31, and 33-35 are rejected under 35 U.S.C. 102(a) as anticipated by Collier et al. WO 99/42473.

Applicants note that amended claims 1 and 6 and new claims 52-64 are directed to SEQ ID NOs:8, 10, 11, 13, and 16, each of which feature anthrax toxin B moieties containing the D425K mutation. Applicants respectfully request withdrawal of each of the rejections for anticipation cited above.

Rejections under 35 U.S.C. § 101

Claims 1-4, 12-20, 40, 41, 50, and 51 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. As suggested by the Examiner, the claims now recite that the B moiety is "purified." Applicants now respectfully request withdrawal of this §101 rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 12, 30, 33, 40, 41, and 47 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Applicants note that claims 12, 30, 33, 40, 41, and 47 have been cancelled. Claim 1 is directed to anthrax toxin B moieties containing defined sequences and; therefore, Applicants respectfully request that this rejection be withdrawn.

## CONCLUSION

In view of the foregoing, all of the pending claims in this case are believed to be in condition for allowance. If the Examiner has any questions or determines that any further action is desirable to place this application in even better condition for issue, the Examiner is encouraged to telephone Applicants' undersigned representative at the number listed below.

Enclosed is a petition to extend the period for replying for two months, to and including January 8, 2004.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: January 8, 2004

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